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EXAMINER

LEUNG, JENNIFER A

ART UNIT	PAPER NUMBER
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1764

DATE MAILED: 09/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/932,277

Applicant(s)

SEEBERGER ET AL.

Examiner

Jennifer A. Leung

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 30 is/are rejected.
- 7) ☒ Claim(s) 29 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Response to Amendment

1. Applicant's amendment submitted on June 27, 2005 has been received and carefully considered. Claims 31-58 are cancelled. Claims 1-30 remain active.

Response to Arguments

2. Applicant's arguments filed on June 27, 2005 have been fully considered but they are not persuasive. Beginning on page 6, under the paragraph numbered 4, Applicants argue,

“Whereas an automated means for synthesizing oligonucleotides was known, an automated means for synthesizing oligosaccharides was for a long time considered unattainable by those of ordinary skill in the art due to the complex nature of saccharide chemistry... First, monosaccharides have up to four sites by which the chain may be extended. Second, or linkages can be formed at each anomeric center. Thus, saccharide chemistry requires multiple protection and deprotection steps. Coassin discloses the automation of peptide synthesis, but does not enable automated oligosaccharide synthesis. The enabled scope of Coassin's automated apparatus does not teach all of the limitations of claim 1... Therefore, the Applicants contend that one of ordinary skill in the art would not have had a reasonable expectation of success in a program aimed at developing the claimed apparatus for automated synthesis based on the combination of Kahne and Coassin.”

Similar arguments are made by Applicants with respect to the combination of Toth et al. and Coassin (see Response, beginning on page 9, under the paragraph numbered 7). However, the Examiner respectfully disagrees and maintains her rejection.

The difficulties encountered in oligosaccharide synthesis are due largely to the complex nature of the “chemistry”, and not the availability of mechanical means or “apparatus” for performing the chemistry. As mentioned above, the synthesis of oligosaccharides was for a long

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time considered unattainable due challenges in the “chemistry”, namely, “monosaccharides have up to four sites by which the chain may be extended” and “linkages can be formed at each anomeric center.” The success in the synthesis of oligosaccharides thus lies in the development of the “chemistry”, e.g., the availability of resins having an appropriate functionality to form the appropriate linkages, etc. The well-known difficulties encountered in the chemistry of oligosaccharide synthesis are further elaborated by Kahne, column 6, line 26, to column 8, line 27. In particular, Kahne cites the work of Frechet and Schuerch, which outlined the key requirements for successful solid-phase oligosaccharide synthesis:

“... *First*, the resin must be compatible with the reaction conditions. *Second*, the solid support must contain appropriate functionality to provide a link to the glycosidic center (or elsewhere), which link is inert to the reaction conditions but can be easily cleaved to remove the oligosaccharide upon completion of the synthesis. *Third*, appropriate protecting group schemes must be worked out so that particular hydroxyls can be selectively unmasked for the next coupling reaction... *Fourth*, the glycosylation reactions should be efficient, mild, and go to completion to avoid failure sequences. *Fifth*, the stereochemistry of the anomeric center must be maintained during the coupling cycles and should be predictable based on the results obtained in solution for any given donor/acceptor pair. *Sixth*, cleavage of the permanent blocking groups and the link to the polymer must leave the oligosaccharide intact.” (column 6, line 53 to column 7, line 3).

Each of these six criteria deal with the “chemistry” of oligosaccharide synthesis. Kahne (column 7, lines 16-23) further states that the difficulties encountered,

“... have been attributed to the fact that reaction kinetics on the solid phase are slower than they are in solution... The consequence of such unfavorable kinetics is that most glycosylation reactions, which may work reasonably well in solution, simply do not work well on a solid phase both in terms of stereochemical control and yield.”

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Again, these difficulties are “chemistry” related.

Apparatus for enabling “multiple protection and deprotection steps” in the solid-phase, however, have long been available in the art. This was evidenced by Coassin (see rejection below). As can be seen in FIG. 1 of Coassin, the exemplary apparatus contains numerous reagent reservoirs and flow components which all enable to the apparatus to perform a multitude of synthesis steps, depending on the desired chemistry. And in particular, Coassin (column 2, lines 54-60, with emphasis added) expressly states that the apparatus is inherently capable of performing oligosaccharide synthesis:

“While the present invention is described in the context of DNA synthesis, it is to be understood that the present invention can be implements for other chemical processes, e.g., peptide and protein synthesis, protein sequencing and oligosaccharide synthesis and sequencing, as well as any system requiring integrated delivery of different reagents..

In addition, the fact that Kahne et al. discloses success in the synthesis of oligosaccharides using a relatively simple apparatus with a manual feed of reagents (see FIG. 5A, 5B; column 29, line 42 to column 32, line 43) would suggest to one of ordinary skill in the art that a more complex apparatus having a means for automated delivery of reagents, such as the apparatus taught by Coassin, would provide at least an equal expectation of success, if not an even greater expectation of success.

Beginning on page 8, under the paragraph numbered 6, Applicants argue,

“Andrade et al. is not available as prior art under 35 USC §103(a) because the article does not qualify as prior art under any section of 35 USC §102... The Organic Letters article published by Andrade et al. was published on the Internet on October 28, 1999. Therefore, the Andrade et al. article is not prior art under 35 USC §102(b) because it was not published more than 1 year prior to the earliest effective filing date (August 18, 2000)

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of the instant application.”

Similar arguments are made beginning on page 9, under the paragraph numbered 8.

The Examiner has withdrawn the rejection of claim 29 because the publication discloses that the use of an octenediol functionalized resin, namely a “novel, versatile octenediol linker” (page 2, first column, second paragraph) is the work in which the publication date of October 28, 1999 applies. However, the Examiner maintains that the Andrade et al. publication qualifies as prior art for the remaining claims; i.e., claims 10, 11, 20, 21, 27, 28 and 30. As disclosed on page 1, in the second column, the development of solid phase synthesis involving “trichloroacetimidates” was made more than one year prior to the earliest effective filing date, as indicated by footnote 8 (i.e., the work was completed by (a) Yan et al. in 1994, as well as Liang et al. in 1996). In addition, the development of solid phase synthesis involving “glycosyl phosphates” (page 2, first column, second paragraph) was disclosed by Applicants more than one year prior to the earliest effective filing date, as indicated by footnote 14 (i.e., the work was published on May 29, 1999). A copy of the citation in footnote 14 has been provided.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-4, 8, 9, 12-14, 17-19, 22 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahne (US 5,635,612) in view of Coassin (US 5,405,585).

Regarding claims 1, 2, 12-14, 17-19 and 22, Kahne discloses a process for synthesizing oligosaccharides on a solid phase support (column 29, line 42 to column 32, line 42; column 53, line 25 to column 54, line 8; column 56, lines 15-38), wherein the process comprises the steps of:

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providing at least one insoluble resin bead (i.e., a support comprising a resin of insoluble polymer that has sites for attaching a glycosyl acceptor via a readily cleavable organic linkage, of which a bead form is well known; column 29, line 44 to column 30, line 23); providing a saccharide donor solution to the reaction vessel (i.e., a glycosyl donor solution comprising a glycosyl sulfoxide; column 31, lines 12-20); providing an activating reagent solution (i.e., suitable activating agents including, but not limited to, an alkyl- or arylsilyl triflate (e.g., trimethylsilyl triflate), an alkyl- or arylsulfonyl triflate, and an alkyl- or arylselenenyl triflate, of which silyl triflate is a well known equivalent and suitable activating agent; column 31, lines 28-53); providing a deblocking reagent solution (i.e., for conducting cleavage, or selective removal of protecting groups, via well known processes of debenzylation, acidic hydrolysis of benzylidenes or acetonates, basic hydrolysis of esters, removal of silyl groups with fluoride or under acidic conditions; column 30, lines 6-23; column 32, lines 6-19; column 56, lines 16-24); providing a solvent (i.e., solvents including, but not limited to, methylene chloride, THF and methanol; column 31, lines 1-11; column 32, lines 6-13); and providing a blocking reagent solution (i.e., for conducting selective addition of protecting groups, via well known processes of benzylation, benzylidenation, acetonation, esterification, and carbo- or silylethentication of sugars; column 30, lines 6-23; column 32, lines 6-19; column 56, lines 16-24);

Kahne discloses a suitable apparatus for conducting the process of synthesizing oligosaccharides, wherein the apparatus comprises a reaction vessel for containing the least one insoluble resin

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bead, the reaction vessel comprising an inlet for the manual addition of solvent and dissolved reagents via canula or syringe needle to the reaction chamber (see FIG. 5A, 5B; column 30, lines 24-68). Kahne further discloses, "[t]here may be many variations on the general apparatus," (column 30, line 30); however, Kahne is silent as to the apparatus further comprising a means for automated delivery of the solvent and dissolved reagents to the reactor chamber, said automated delivery means comprising:

- at least one donor vessel for containing the saccharide donor solution;
- at least one activator vessel for containing the activating reagent solution;
- at least one deblocking vessel for containing the deblocking reagent solution;
- at least one solvent vessel for containing the solvent;
- at least one blocking vessel for containing the blocking reagent solution;
- a solution transfer system capable of transferring the saccharide donor solution, activating reagent solution, deblocking reagent solution, and solvent to the reaction vessel; and
- a computer for controlling the solution transfer system.

In any event, it would have been obvious for one of ordinary skill in the art at the time the invention was made to provide such automated delivery means to the apparatus of Kahne, on the basis of suitability for the intended use, because the provision of mechanical or automated means to replace manual activity was held to have been obvious. *In re Venner* 120 USPQ 192 (CCPA 1958); *In re Rundell* 9 USPQ 220 (CCPA 1931). Coassin teaches an automated delivery means suitable for delivering solvent and reagents to a reactor for conducting solid phase synthesis of oligosaccharides (column 2, line 54 to column 4, line 9), wherein the means comprises a plurality of vessels (i.e., reservoirs 11-21; FIG. 1), each containing an appropriate chemical reagent or solvent for conducting a particular chemical process. The means further comprises a solution transfer system (i.e., comprising tubings 32; valves 41-48) capable of transferring the various

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reagents or solvents to the reactor vessel (i.e., reactor vessel 50) and a computer for controlling the solution transfer system (i.e., controller 80). The automated delivery means allows for the handling of several types of fluids in a flow system while reducing chemical reagent cross contamination and simplifying system design and control, as taught by Coassin.

Regarding claims 3, 4, 8, 9 and 26, Kahne (FIG. 5A; column 30, lines 62-65; column 31, lines 28-39) discloses a temperature control unit (labeled, "oil bath or cold bath") capable of maintaining the reaction vessel at a temperature of -78 °C. In an example, Kahne further discloses steps of cooling the reaction vessel to temperatures of 0 °C and -60 °C (column 53, line 25 to column 54, line 9). Although the claimed temperature ranges are not recited in the Kahne reference, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select an appropriate temperature for the reaction vessel in the apparatus of Kahne, on the basis of suitability for the intended use, because the temperature control unit is inherently capable of temperature adjustment, as evidenced by the multiple temperatures disclosed above, and furthermore, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art, *In re Aller*, 105 USPQ 233. Additionally, Kahne is silent as to the temperature control unit having its temperature adjustment being controlled by a computer. In any event, it would have been obvious for one of ordinary skill in the art at the time the invention was made to provide a computer for controlling the temperature control unit in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the provision of computers to automatically regulate the temperature of temperature control units is well known in the art.

Regarding claims 15 and 16, although Kahne is silent as to the deblocking solution

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comprising sodium methoxide or hydrazine, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select sodium methoxide or hydrazine for the deblocking reagent solution in the modified apparatus of Kahne, on the basis of suitability for the intended use, because such reagents are well known deblocking reagents in the art.

Regarding claims 23-25, although Kahne is silent as to the blocking reagent solution comprising a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid for the blocking reagent solution in the modified apparatus of Kahne, on the basis of suitability for the intended use, because such reagents are well known blocking reagents in the art.

4. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahne (US 5,635,612) in view of Coassin (US 5,405,585), as applied to claims 1 and 3 above, and further in view of Lapluye et al. (US 5,466,608).

Regarding claim 5, Kahne is silent as to the temperature control unit comprising a means for measuring the internal temperature of the reactor vessel. Lapluye et al. an apparatus for the synthesis of macromolecules, including oligosaccharides, wherein the internal temperature of a reactor 10 is measured by a temperature probe 36 (FIG. 1; column 4, lines 32-47; column 6, line 63 to column 7, line 1). It would have been obvious for one of ordinary skill in the art at the time the invention was made to provide a means for measuring the internal temperature of the reactor vessel in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the means for measuring the internal temperature would allow for a user to monitor the development of an ongoing reaction by detecting variations in temperature to determine the end

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of the reaction, as taught by Lapluye et al. (column 2, lines 23-43).

Regarding claim 6, Kahne is silent as to whether the reactor and bath structure (FIG. 5A) may comprise a double-wall structure forming two cavities, wherein a first cavity accommodates the synthesis of oligosaccharides and a second cavity accommodates a coolant of the temperature control unit. Lapluye et al. teaches a reactor for the synthesis of macromolecules, including oligosaccharides, wherein the reactor comprises a double-wall structure forming two cavities (i.e., a cylindrical double wall vessel **16** defining an outer cavity for thermoregulated liquid **18** and an inner cavity for accommodating the synthesis of oligosaccharides on resin **12**; FIG. 1). It would have been obvious for one of ordinary skill in the art at the time the invention was made to substitute a reactor comprising a double-wall structure for the reactor and bath structure in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the substitution of known equivalent structures involves only ordinary skill in the art. *In re Fout* 213 USPQ 532 (CCPA 1982); *In re Susi* 169 USPQ 423 (CCPA 1971); *In re Siebentritt* 152 USPQ 618 (CCPA 1967); *In re Ruff* 118 USPQ 343 (CCPA 1958).

Regarding claim 7, Lapluye et al. is silent as to the double wall structure **16** of the reaction vessel being comprised of glass. In any event, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select glass for the material of the double wall structure in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the use glass for reactor materials is well known in the art, since the material is inherently inert to the fluids and reactants.

5. Claims 10, 11, 20, 21, 27, 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahne (US 5,635,612) in view of Coassin (US 5,405,585), as applied to claim

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1 above, and further in view of Andrade et al. (Organic Letters, 1999, vol. 1, no. 11, 1811-1814) and Plante et al. (Organic Letters 1999, vol. 1, no. 2, 211-214).

Regarding claims 10 and 11, although Kahne is silent as to whether a glycosyl trichloroacetimidate or phosphate may be used for the saccharide donor solution, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a glycosyl trichloroacetimidate or a glycosyl phosphate for the saccharide donor solution in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the substitution of known equivalent structures involves only ordinary skill in the art. *In re Fout* 213 USPQ 532 (CCPA 1982); *In re Susi* 169 USPQ 423 (CCPA 1971); *In re Siebentritt* 152 USPQ 618 (CCPA 1967); *In re Ruff* 118 USPQ 343 (CCPA 1958). As evidenced by Andrade et al., glycosyl trichloroacetimidates (refer to citation 8, to (a) Yan et al., 1994, or (b) Liang et al., 1996) and glycosyl phosphates (refer to citation 14, to Plante et al., with a prior art publication date of May 29, 1999), in addition to the glycosyl sulfoxides as used in the method of Kahne, are known saccharide donors used for synthesizing oligosaccharides (page 1, column 1, first paragraph, to page 2, column 1, third paragraph).

Regarding claims 20, 21, 27 and 28, although Kahne is silent as to the specifically claimed combination of reagents and solvents, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to an appropriate combination of reagents and solvents well known for the synthesis of oligosaccharides in the modified apparatus of Kahne, on the basis of suitability for the desired oligosaccharide structure to be synthesized, in absence of showing any unexpected results thereof.

Regarding claim 30, although Kahne is silent as to whether the organic linker may be

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comprised of a glycosyl phosphate, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to select a glycosyl phosphate for the organic linker in the modified apparatus of Kahne, on the basis of suitability for synthesizing oligosaccharides from glycosyl phosphate saccharide donors, because such linkers are well known in the art.

6. Claims 1, 2, 10, 12-20 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toth et al. (WO 98/08799) in view of Coassin (US 5,405,585).

Regarding claims 1, 2, 10, 12, 14-20 and 22, Toth et al. discloses a process of synthesizing oligosaccharides, wherein the process components are to be provided in an apparatus of "kit" form, wherein the "kit" may include a resin-linker-saccharide support or resin-linker support and, optionally,

"... one or more further reagents such as protecting agents, deprotecting agents, and/or solvents suitable for solid phase or combinatorial synthesis. The person skilled in the art will be aware of suitable further reagents. Different types of kit can then be chosen according to the desired use." (page 9, line 29 to page 10, line 5).

Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to provide a kit comprising:

at least one insoluble resin bead (e.g., a support comprising any resin that swells in water and/or an organic solvent, an organic linker, and a sugar attached to the resin-linker unit such as an unprotected, partially protected or fully protected glycoside; page 10, lines 5-11; page 11, lines 14-18; page 5, line 34 to page 7, line 15; page 14, line 28 to page 15, line 9); saccharide donor solutions (e.g., a donor solution comprising any activated sugar, including but not limited to trichloroacetimidates; column 11, lines 19-30);

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activating reagent solutions (e.g., trimethylsilyl trifluoromethanesulfonate; page 17, lines 5-9); deblocking reagent solutions (e.g., deprotecting agents, hydrazine, sodium methoxide; page 12, lines 4-16; page 16, lines 12-25; page 17, lines 20-23); solvents (e.g., dichloromethane, MeOH, THF; page 17, line 8 and line 22; page 18, line 30); and blocking reagent solutions (i.e., protecting agents; page 9, line 37).

As described in Examples 1-52, it appears that the disclosed reagents and solvents of the kit are used to manually synthesize a variety of oligosaccharides (i.e., no mechanical means are disclosed). Thus, Toth et al. is silent as to whether the oligosaccharide synthesis may be automated by conducting the synthesis in an apparatus comprising:

- a reaction vessel for containing the at least one insoluble resin bead;
- at least one donor vessel containing the saccharide donor solution;
- at least one activator vessel containing the activating reagent solution;
- at least one deblocking vessel containing the deblocking reagent solution;
- at least one solvent vessel containing the solvent;
- a solution transfer system capable of transferring the saccharide donor solution, activating reagent solution, deblocking reagent solution, and solvent to the reaction vessel; and
- a computer for controlling the solution transfer system.

In any event, it would have been obvious for one of ordinary skill in the art at the time the invention was made to provide means for automating the synthesis of oligosaccharides in the process of Toth et al., on the basis of suitability for the intended use, because the provision of mechanical or automated means to replace manual activity was held to have been obvious. *In re Venner* 120 USPQ 192 (CCPA 1958); *In re Rundell* 9 USPQ 220 (CCPA 1931). Coassin teaches an apparatus suitable for conducting the synthesis of oligosaccharides (column 2, line 54 to column 4, line 9), wherein the apparatus comprises a plurality of vessels (i.e., reservoirs 11-21;

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FIG. 1), each containing an appropriate chemical reagent or solvent for conducting a particular chemical process. The apparatus further comprises a solution transfer system (i.e., comprising tubings 32; valves 41-48) capable of transferring the various reagents or solvents to the reactor vessel (i.e., reactor vessel 50) and a computer for controlling the solution transfer system (i.e., controller 80). The automated apparatus allows for the handling of several types of fluids in a flow system while reducing chemical reagent cross contamination and simplifying system design and control, as taught by Coassin.

Regarding claim 13, although Toth et al. is silent as to the activating reagent solution comprising silyl trifluoromethanesulfonate, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select silyl trifluoromethanesulfonate for the activating agent solution in the modified apparatus of Toth et al., on the basis of suitability for the intended use, because the use of such reagent as an activating reagent is well known, and the substitution of known equivalents merely involves routine skill in the art.

Regarding claim 20, although Toth et al. is silent as to the specifically claimed combination of reagents and solvents, Toth et al. discloses a combination of, "... one or more further reagents such as protecting agents, deprotecting agents, and/or solvents suitable for solid phase or combinatorial synthesis. The person skilled in the art will be aware of suitable further reagents. Different types of kit can then be chosen according to the desired use." (page 9, line 29 to page 10, line 5). Thus, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to an appropriate combination of reagents and solvents well known for the synthesis of oligosaccharides in the modified apparatus of Toth et al., on the basis of suitability for the desired oligosaccharide structure to be synthesized, in

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absence of showing any unexpected results thereof.

Regarding claims 23-25, although Toth et al. is silent as to the blocking reagent solution comprising a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid for the blocking reagent solution in the modified apparatus of Toth et al., on the basis of suitability for the intended use, because such reagents are well known blocking reagents in the art.

7. Claims 11, 21 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toth et al. (WO 98/08799) in view of Coassin (US 5,405,585), as applied to claims 1 and 2 above, and further in view of Andrade et al. (Organic Letters, 1999, vol. 1, no. 11, 1811-1814) and Plante et al. (Organic Letters 1999, vol. 1, no. 2, 211-214).

Regarding claim 11, although Toth et al. is silent as to the saccharide donor solution comprising a glycosyl phosphate, Toth et al. discloses that, "The building block mono- or oligosaccharide donors may be any activated sugar, *including but not limited to...*" the various recited saccharide donors (see page 11, lines 19-30). Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a glycosyl phosphate for the saccharide donor solution in the modified apparatus of Toth et al., on the basis of suitability for the intended use, because the substitution of known equivalents involves only ordinary skill in the art. As evidenced by Andrade et al., glycosyl phosphates (refer to citation 14, to Plante et al., with a prior art publication date of May 29, 1999), in addition to the trichloroacetimidates used in the method of Toth et al., are known donors used for synthesizing oligosaccharides (page 1, column 1, first paragraph, to page 2, column 1, third paragraph).

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Regarding claim 21, although Toth et al. is silent as to the specifically claimed combination of reagents and solvents, including a glycosyl phosphate donor (see Andrade above), Toth et al. discloses a combination of, "... one or more further reagents such as protecting agents, deprotecting agents, and/or solvents suitable for solid phase or combinatorial synthesis. The person skilled in the art will be aware of suitable further reagents. Different types of kit can then be chosen according to the desired use." (page 9, line 29 to page 10, line 5). Thus, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to an appropriate combination of reagents and solvents well known for the synthesis of oligosaccharides in the modified apparatus of Toth et al., on the basis of suitability for the desired oligosaccharide structure to be synthesized, in absence of showing any unexpected results thereof.

Regarding claim 30, although Toth et al. is silent as to whether the organic linker may be comprised of a glycosyl phosphate, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to select a glycosyl phosphate for the organic linker in the modified apparatus of Toth et al., on the basis of suitability for synthesizing oligosaccharides from glycosyl phosphate saccharide donors, because such linkers are well known in the art.

Allowable Subject Matter

8. Claim 29 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The following is a statement of reasons for the indication of allowable subject matter:

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The prior art does not disclose or adequately teach the claimed apparatus comprising vessels containing the combination of reactants as positively recited; in particular, the prior does not disclose a reaction vessel containing at least on insoluble resin bead comprised of an octenediol functionalized resin.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

* * *

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Leung whose telephone number is (571) 272-1449. The examiner can normally be reached on 8:30 am - 5:30 pm M-F, every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Glenn A. Caldarola can be reached on (571) 272-1444. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer A. Leung

September 18, 2005 *gde*

Hien Tran

**HIEN TRAN
PRIMARY EXAMINER**